

WHAT IS CLAIMED IS:

1. A method of modulating the level or activity of a chemokine, said method comprising:
modulating in an endothelial cell the level or activity of the NF-HEV polypeptide or a biologically active fragment thereof, thereby modulating the level or activity of said chemokine.
2. The method of Claim 1, wherein the level or activity of said NF-HEV polypeptide or a biologically active fragment thereof is modulated by altering the expression of a nucleic acid encoding said NF-HEV polypeptide or a biologically active fragment thereof in said cell.
3. The method of Claim 1, wherein the level or activity of said NF-HEV polypeptide or a biologically active fragment thereof is modulated by providing said cell with a compound.
4. The method of Claim 1, wherein said endothelial cell is an HEVEC.
5. Then method of Claim 4, wherein said cell is a mammalian cell.
6. The method of Claim 5, wherein said HEVEC cell is a human cell.
7. The method of Claim 1, wherein in said chemokine is a pro-inflammatory chemokine.
8. The method of Claim 7, wherein said pro-inflammatory chemokine is selected from the group consisting of XCL1/GRO α , CXCL2/GRO β , CXCL6, CXCL8/IL8 and CCL2/MCP1.
9. The method of Claim 7, wherein the level or activity of said pro-inflammatory chemokine is reduced.
10. The method of Claim 1, wherein the level or activity of said NF-HEV polypeptide or a biologically active fragment thereof is reduced.
11. The method of Claim 10, wherein the level or activity of said NF-HEV polypeptide or a biologically active fragment thereof is reduced by reducing the expression of a nucleic acid encoding said NF-HEV polypeptide or a biologically active fragment thereof in said cell.
12. The method of Claim 11, wherein the expression of a nucleic acid encoding said NF-HEV polypeptide or a biologically active fragment thereof is reduced by providing an antisense nucleic acid complementary to at least a portion of said NF-HEV polypeptide or a biologically active fragment thereof.
13. The method of Claim 10, wherein the level or activity of said NF-HEV polypeptide or a biologically active fragment thereof is reduced by reducing the activity or level of a pro-inflammatory cytokine.
14. A method of reducing the level or activity of a chemokine, said method comprising:
reducing in a cell the level or activity of the NF-HEV polypeptide or a biologically active fragment thereof, thereby reducing the level or activity of a chemokine.

15. The method of Claim 14, wherein reducing the level or activity of the NF-HEV polypeptide or a biologically active fragment thereof does not include reducing the level or activity of a pro-inflammatory cytokine.

16. The method of Claim 14, wherein the level or activity of the NF-HEV polypeptide or a biologically active fragment thereof is reduced by providing to said cell a compound that reduces the level or activity of the NF-HEV polypeptide or a biologically active fragment thereof.

17. The method of Claim 16, wherein the compound is an antisense nucleic acid that is complementary to at least a portion of a nucleic acid encoding NF-HEV.

18. The method of Claim 16, wherein the compound is an siRNA specific for at least a portion of a nucleic acid encoding NF-HEV.

19. The method of Claim 14, wherein in said chemokine is a pro-inflammatory chemokine.

20. The method of Claim 19, wherein said pro-inflammatory chemokine is selected from the group consisting of XCL1/GRO α , CXCL2/GRO β , CXCL6, CXCL8/IL8 and CCL2/MCP1.

21. The method of Claim 14, wherein the cell is an endothelial cell.

22. The method of Claim 21, wherein the cell is a HEVEC cell.

23. A method of ameliorating symptoms of a condition associated with inflammation, said method comprising:

identifying a subject having symptoms of a condition associated with inflammation;

and

modulating in said subject the level or activity of the NF-HEV polypeptide or a biologically active fragment thereof, thereby ameliorating symptoms of a condition associated with inflammation.

24. The method of Claim 23, wherein the level or activity of said NF-HEV polypeptide or a biologically active fragment thereof is modulated by altering the expression of a nucleic acid encoding said NF-HEV polypeptide or a biologically active fragment thereof.

25. The method of Claim 23, wherein the level or activity of said NF-HEV polypeptide or a biologically active fragment thereof is modulated by administering a compound to said subject.

26. The method of Claim 23, wherein modulating the level or activity of said NF-HEV polypeptide or a biologically active fragment thereof modulates the level or activity of a pro-inflammatory chemokine.

27. The method of Claim 26, wherein said pro-inflammatory chemokine is selected from the group consisting of XCL1/GRO α , CXCL2/GRO β , CXCL6, CXCL8/IL8 and CCL2/MCP1.

28. The method of Claim 26, wherein the level or activity of said pro-inflammatory chemokine is reduced.

29. The method of Claim 23, wherein the level or activity of said NF-HEV polypeptide or a biologically active fragment thereof is reduced.

30. The method of Claim 29, wherein the level or activity of said NF-HEV polypeptide or a biologically active fragment thereof is reduced by reducing the expression of a nucleic acid encoding said NF-HEV polypeptide or a biologically active fragment thereof.

31. The method of Claim 30, wherein the expression of a nucleic acid encoding said NF-HEV polypeptide or a biologically active fragment thereof is reduced by providing an antisense nucleic acid complementary to at least a portion of said NF-HEV polypeptide or a biologically active fragment thereof.

32. The method of Claim 29, wherein the level or activity of said NF-HEV polypeptide or a biologically active fragment thereof is reduced by reducing the activity or level of a pro-inflammatory cytokine.

33. A method of ameliorating the symptoms of a condition associated with inflammation, said method comprising modulating the level of transcription of at least one promoter responsive to an NF-HEV polypeptide or biologically active fragment thereof.

34. The method of Claim 33, wherein the level of transcription of said at least one promoter responsive to an NF-HEV polypeptide or biologically active fragment thereof is reduced.

35. The method of Claim 33, wherein modulating the level or activity of said promoter modulates the level or activity of a pro-inflammatory chemokine.

36. The method of Claim 35, wherein said pro-inflammatory chemokine is selected from the group consisting of XCL1/GRO α , CXCL2/GRO β , CXCL6, CXCL8/IL8 and CCL2/MCP1.

37. The method of Claim 35, wherein the level or activity of said pro-inflammatory chemokine is reduced.

38. A nucleic acid selected from the group consisting of:

(i) a nucleic acid molecule encoding a polypeptide comprising an amino acid sequence selected from the group of sequences consisting of SEQ ID NOs: 4-5;

(ii) a nucleic acid molecule comprising a nucleic acid sequence selected from the group of sequences consisting of SEQ ID NOs: 1-2, or a sequence complementary thereto;

(iii) a nucleic acid molecule the complementary strand of which hybridizes under stringent conditions to a nucleic acid as defined in (i) and (ii); and

(iv) a nucleic acid the sequence of which is degenerate as a result of the genetic code to a sequence of a nucleic acid as defined in (i), (ii) and (iii).

39. The nucleic acid of Claim 38, wherein said nucleic acid is operably linked to a promoter.

40. An expression cassette comprising the nucleic acid of Claim 39.

41. A host cell comprising the expression cassette of Claim 40.

42. An isolated nucleic acid comprising a nucleotide sequence encoding:

i) a polypeptide comprising an amino acid sequence having at least about 80% identity to a sequence selected from the group consisting of the polypeptides of SEQ ID NOs: 4-5, and the polypeptides encoded by the nucleic acid of SEQ ID NOs: 1-2; or

ii) a biologically active fragment of said polypeptide.

43. The nucleic acid of Claim 42, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of the sequences shown as SEQ ID NOs: 4-5 and the polypeptides encoded by the nucleic acid of SEQ ID NOs: 1-2.

44. A method of making a NF-HEV polypeptide, said method comprising:

a) providing a population of host cells comprising a nucleic acid encoding said NF-HEV protein having an amino acid sequence selected from the group consisting of SEQ ID NOs: 4-5 and sequence having at least 80% amino acid identity to SEQ ID NOs: 4-5; and

b) culturing said population of host cells under conditions conducive to the expression of said recombinant nucleic acid, whereby said polypeptide is produced within said population of host cells.

45. The method of Claim 44, further comprising purifying said polypeptide from said population of cells.

46. An isolated nucleic acid, said nucleic acid comprising a nucleotide sequence having at least about 80% identity over at least about 100 nucleotides to a sequence selected from the group consisting of SEQ ID NOs: 1-2 and sequences complementary to SEQ ID NOs: 1-2.

47. The nucleic acid of Claim 46, wherein said nucleic acid hybridizes under stringent conditions to a nucleic acid having a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-2 and sequences complementary to SEQ ID NOs: 1-2.

48. The nucleic acid of Claim 46, wherein identity is determined using an algorithm selected from the group consisting of NBLAST with the parameters score=100 and wordlength=12, Gapped BLAST with the default parameters of NBLAST, and BLAST with the default parameters of NBLAST.

49. A biologically active NF-HEV polypeptide encoded by the nucleic acid of Claim 38 or 42.

50. A biologically active isolated NF-HEV polypeptide or fragment thereof, said polypeptide comprising an amino acid sequence having at least about 80% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NOs: 4-5.

51. The polypeptide of Claim 50, wherein said polypeptide is selectively bound by an antibody raised against an antigenic polypeptide, or antigenic fragment thereof, said antigenic polypeptide comprising a polypeptide selected from the group consisting of SEQ ID NOs: 4-5.

52. The polypeptide of Claim 50, wherein said polypeptide comprises a polypeptide selected from the group consisting of SEQ ID NOs: 4-5.

53. An antibody that selectively binds to the polypeptide of Claim 49.

54. A method of determining whether a NF-HEV nucleic acid or polypeptide is expressed within a biological sample, said method comprising the steps of:

a) contacting said biological sample with a polynucleotide that hybridizes under stringent conditions to a nucleic acid of Claim 38 or a detectable polypeptide that selectively binds to the polypeptide of Claim 50 or Claim 52; and

b) detecting the presence or absence of hybridization between said polynucleotide and an RNA species within said sample, or the presence or absence of binding of said detectable polypeptide to a polypeptide within said sample, wherein a detection of said hybridization or of said binding indicates that said NF-HEV is expressed within said sample.

55. The method of Claim 54, wherein said polynucleotide is a primer, and wherein said hybridization is detected by detecting the presence of an amplification product comprising said primer sequence.

56. The method of Claim 54, wherein said detectable polypeptide is an antibody.

57. A method of determining whether a mammal has an elevated or reduced level of NF-HEV expression, said method comprising the steps of:

a) providing a biological sample from said mammal; and

b) comparing the amount of a NF-HEV polypeptide of Claim 50 or Claim 52 or of a NF-HEV RNA species encoding a polypeptide of Claim 50 within said biological sample with a level detected in or expected from a control sample, wherein an increased amount of said NF-HEV polypeptide or said NF-HEV RNA species within said biological sample compared to said level detected in or expected from said control sample indicates that said mammal has an elevated level of NF-HEV expression, and wherein a decreased amount of said

NF-HEV polypeptide or said NF-HEV RNA species within said biological sample compared to said level detected in or expected from said control sample indicates that said mammal has a reduced level of NF-HEV expression.

58. A method of identifying a candidate inhibitor of a NF-HEV polypeptide, said method comprising:

- a) contacting a NF-HEV polypeptide according to Claim 50 or Claim 52 or a fragment thereof which comprises a contiguous span of at least 6 contiguous amino acids of the polypeptide according to Claim 50 or Claim 52 with a test compound; and
- b) determining whether said compound selectively binds to said polypeptide, wherein a determination that said compound selectively binds to said polypeptide indicates that said compound is a candidate inhibitor of said polypeptide.

59. The method of Claim 58, wherein a determination that said compound selectively binds to said polypeptide indicates that said compound is a candidate compound for the treatment of a chronic inflammatory disorder.

60. A method of identifying a candidate inhibitor of a NF-HEV polypeptide of Claim 50 or Claim 52 or a fragment comprising a contiguous span of at least 6 contiguous amino acids of the polypeptide according to Claim 50 or Claim 52, said method comprising:

- a) contacting said polypeptide with a test compound; and
- b) determining whether said compound selectively inhibits at least one activity of said polypeptide, wherein a determination that said compound selectively inhibits at least one activity of said polypeptide indicates that said compound is a candidate inhibitor of said polypeptide.

61. The method of Claim 60, wherein a determination that said compound selectively inhibits said at least one biological activity of said polypeptide indicates that said compound is a candidate compound for the treatment of a chronic inflammatory disorder.

62. A method of identifying a candidate NF-HEV inhibitor, said method comprising:

- a) providing a cell comprising a NF-HEV polypeptide or a fragment comprising at least 6 consecutive amino acids thereof;
- b) contacting said cell with a test compound; and
- c) determining whether said compound selectively inhibits at least one NF-HEV activity, wherein a determination that said compound selectively inhibits activity of said polypeptide indicates that said compound is a candidate inhibitor of said polypeptide.

63. The method of Claim 62, wherein a determination that said compound selectively inhibits said at least one biological activity of said polypeptide indicates that said compound is a candidate compound for the treatment of a chronic inflammatory disorder.

64. The method of Claim 62, wherein step (a) comprises introducing a nucleic acid comprising the nucleotide sequence encoding said NF-HEV polypeptide according to any one of Claims 38, 39, 42 or 43 into said cell.

65. The method of any of Claims 58 to 64, wherein said NF-HEV activity comprises modulating gene expression in an endothelial cell.

66. The method of any of Claims 58 to 64, wherein said NF-HEV activity comprises modulating the inflammatory potential of an endothelial cell.

67. The method of any of Claims 58 to 64, wherein said NF-HEV activity comprises modulating the phenotype of an endothelial cell.

68. The method of any of Claims 58 to 64, wherein said NF-HEV activity comprises regulating HEV-like vessel development or maintenance.

69. The method of any of Claims 58 to 64, wherein said NF-HEV activity comprises modulating the differentiation or proliferation of an endothelial cell.

70. The method of any of Claims 58 to 64, wherein said NF-HEV polypeptide or fragment thereof comprises a homeodomain-like helix-turn-helix (HTH) DNA-binding domain.

71. The method of any of Claims 58 to 64, wherein said NF-HEV polypeptide or fragment thereof comprises the amino acid sequence of positions 61 to 78 of SEQ ID NO: 1 or 63 to 80 of SEQ ID NO: 2.

72. A polynucleotide according to any one of Claims 38, 39, 42 or 43 attached to a solid support.

73. An array of polynucleotides comprising at least one polynucleotide according to Claim 72.

74. An array according to Claim 72, wherein said array is addressable.

75. A polynucleotide according to any one of Claims 38, 39, 42 or 43 further comprising a label.

76. A viral composition comprising a recombinant viral vector encoding a NF-HEV protein according to Claims 50 or 52.

77. The composition of Claim 76, wherein said recombinant viral vector is selected from the group consisting of an adenoviral, adeno-associated viral, retroviral, herpes viral, papilloma viral, and hepatitis B viral vector.

78. A method of modulating endothelial cell differentiation comprising modulating the activity of the NF-HEV protein.

79. A method of modulating endothelial cell differentiation comprising modulating the activity of the NF-HEV protein.

80. A method of inducing the differentiation of an endothelial cell comprising contacting a cell with a NF-HEV polypeptide or with a nucleic acid encoding a NF-HEV polypeptide.

81. The method of Claim 80 comprising inducing the differentiation of a HEVEC cell.

82. A method according to Claims 80 or 81, comprising contacting said subject with a recombinant vector encoding a NF-HEV protein according to any one of Claims 43 or 45 operably linked to a promoter that functions in said cell.

83. A method of modulating extravasation of lymphocytes in an individual comprising modulating the activity of the NF-HEV protein in said individual.

84. A method of reducing inflammation in an individual comprising inhibiting the activity of the NF-HEV protein in said individual.

85. A method of increasing extravasation of lymphocytes in an individual comprising increasing the activity of the NF-HEV protein in said individual.

86. A nucleic acid comprising a contiguous span of at least 20 nucleotides of a sequence selected from the group consisting of SEQ ID NOs: 1-2, and sequences complementary to SEQ ID NOs: 1-2.

87. A method of identifying a candidate activator of a NF-HEV polypeptide, said method comprising:

a) contacting a NF-HEV polypeptide according to Claim 50 or Claim 52 or a fragment comprising a contiguous span of at least 6 contiguous amino acids of a polypeptide according to Claim 50 or Claim 52 with a test compound; and

b) determining whether said compound selectively binds to said polypeptide, wherein a determination that said compound selectively binds to said polypeptide indicates that said compound is a candidate activator of said polypeptide.

88. A method of identifying a candidate activator of a NF-HEV polypeptide of Claim 50 or Claim 52 or a fragment comprising a contiguous span of at least 6 contiguous amino acids of a polypeptide according to Claim 50 or Claim 52, said method comprising:

a) contacting said polypeptide with a test compound; and

b) determining whether said compound selectively increases at least one activity of said polypeptide, wherein a determination that said compound selectively increases at least one

activity of said polypeptide indicates that said compound is a candidate inhibitor of said polypeptide.

89. A method of identifying a candidate NF-HEV activator, said method comprising:

a) providing a cell comprising a NF-HEV polypeptide or a fragment comprising at least 6 consecutive amino acids thereof;

b) contacting said cell with a test compound; and

c) determining whether said compound selectively activates at least one NF-HEV biological activity, wherein a determination that said compound selectively activates the activity of said polypeptide indicates that said compound is a candidate activator of said polypeptide.

90. The method of Claim 87 wherein step (a) comprises introducing a nucleic acid comprising the nucleotide sequence encoding said NF-HEV polypeptide according to any one of Claims 38, 39, 42 or 43 into said cell.

91. The method of Claims 87 to 89, wherein said NF-HEV activity comprises modulating gene expression in an endothelial cell.

92. The method of Claims 87 to 89, wherein said NF-HEV activity comprises modulating the inflammatory potential of an endothelial cell.

93. The method of Claims 87 to 89, wherein said NF-HEV activity comprises modulating the phenotype of an endothelial cell.

94. The method of Claims 87 to 89, wherein said NF-HEV activity comprises regulating HEV-like vessel development or maintenance.

95. The method of Claims 87 to 89, wherein said NF-HEV activity comprises modulating the differentiation or proliferation of an endothelial cell.

96. The nucleic acid of Claim 42, wherein polypeptide identity is determined using an algorithm selected from the group consisting of XBLAST with the parameters score=50 and wordlength=3, Gapped BLAST with the default parameters of XBLAST, and BLAST with the default parameters of XBLAST.

97. The polypeptide of Claim 50, wherein identity is determined using an algorithm selected from the group consisting of XBLAST with the parameters score=50 and wordlength=3, Gapped BLAST with the default parameters of XBLAST, and BLAST with the default parameters of XBLAST.

98. An isolated nucleic acid encoding a biologically active NF-HEV polypeptide, said polypeptide comprising an amino acid sequence encoding the DNA-binding domain of the NF-HEV

polypeptide, a biologically fragment thereof, or a polypeptide having at least 80% amino acid identity thereto.

99. An isolated nucleic acid encoding a biologically active NF-HEV polypeptide, said polypeptide comprising the amino acid sequence of amino acid positions 1 to 65 of SEQ ID NO: 4, a biologically fragment thereof, or a polypeptide having at least 80% amino acid identity thereto.

100. An isolated nucleic acid encoding a biologically active NF-HEV polypeptide, said polypeptide comprising the amino acid sequence of amino acid positions 1 to 67 of SEQ ID NO: 5, a biologically fragment thereof, or a polypeptide having at least 80% amino acid identity thereto.

101. An isolated nucleic acid encoding a biologically active NF-HEV polypeptide, said polypeptide comprising the amino acid sequence of amino acid positions 61 to 78 of SEQ ID NO: 4, a biologically fragment thereof, or a polypeptide having at least 80% amino acid identity thereto.

102. An isolated nucleic acid encoding a biologically active NF-HEV polypeptide, said polypeptide comprising the amino acid sequence of amino acid positions 63 to 80 of SEQ ID NO: 5, a biologically fragment thereof, or a polypeptide having at least 80% amino acid identity thereto.

103. An isolated nucleic acid encoding a biologically active NF-HEV polypeptide, said polypeptide comprising the amino acid sequence of amino acid positions 1 to 65 of SEQ ID NO: 1, a biologically fragment thereof, or a polypeptide having at least 80% amino acid identity thereto.

104. A polypeptide comprising a contiguous span of at least 6 amino acids of a sequence selected from the group consisting of SEQ ID NOs: 4-5.

105. The polypeptide of Claim 50, wherein said polypeptide comprises a homeodomain-like helix-turn-helix DNA-binding domain, or a fragment thereof.

106. The polypeptide of Claim 50, wherein said polypeptide comprises a contiguous span of at least 6 amino acids of amino acid positions 1 to 65 of SEQ ID NO: 4.

107. The polypeptide of Claim 50, wherein said polypeptide comprises a contiguous span of at least 6 amino acids of amino acid positions 1 to 67 of SEQ ID NO: 5.

108. The polypeptide of Claim 50, wherein said polypeptide comprises a contiguous span of at least 6 amino acids of amino acid positions 61 to 78 of SEQ ID NO: 5.

109. The polypeptide of Claim 50, wherein said polypeptide comprises a contiguous span of at least 6 amino acids of amino acid positions 63 to 80 of SEQ ID NO: 5.

110. A method of assessing the biological activity of a NF-HEV polypeptide comprising:

(a) providing a NF-HEV polypeptide or a fragment thereof; and

(b) assessing the ability of the NF-HEV polypeptide to induce differentiation of an endothelial cell.

111. A method of assessing the biological activity of a NF-HEV polypeptide comprising:
 - (a) providing a NF-HEV polypeptide or a fragment thereof; and
 - (b) assessing the ability of the NF-HEV polypeptide to modulate gene expression in an endothelial cell.
112. A method of assessing the biological activity of a NF-HEV polypeptide comprising:
 - (a) providing a NF-HEV polypeptide or a fragment thereof; and
 - (b) assessing the DNA binding activity of the NF-HEV polypeptide.
113. The method of Claims 110, 111 or 112, wherein step (a) comprises introducing to a cell a recombinant vector comprising a nucleic acid encoding a NF-HEV polypeptide.
114. The method of Claims 110, 111 or 112, wherein said NF-HEV activity comprises modulating gene expression in an endothelial cell.
115. The method of Claims 110, 111 or 112, wherein said NF-HEV activity comprises modulating the inflammatory potential of an endothelial cell.
116. The method of Claims 110, 111 or 112, wherein said NF-HEV activity comprises modulating the phenotype of an endothelial cell.
117. The method of Claims 110, 111 or 112, wherein said NF-HEV activity comprises regulating HEV-like vessel development or maintenance.
118. The method of Claims 110, 111 or 112, wherein said NF-HEV activity comprises modulating the differentiation or proliferation of an endothelial cell.
119. A method of obtaining a nucleic acid sequence which is recognized by a NF-HEV polypeptide comprising contacting a pool of random nucleic acids with said NF-HEV polypeptide or a portion thereof and isolating a complex comprising said NF-HEV polypeptide and at least one nucleic acid from said pool.
120. The method of Claim 119, wherein said pool of nucleic acids are labeled.
121. The method of Claim 119, wherein said complex is isolated by performing a gel shift analysis.
122. A method of identifying a nucleic acid sequence which is recognized by a NF-HEV polypeptide comprising:
 - (a) incubating a NF-HEV polypeptide with a pool of labelled random nucleic acids;
 - (b) isolating a complex between said NF-HEV polypeptide and at least one nucleic acid from said pool;
 - (c) performing an amplification reaction to amplify the at least one nucleic acid present in said complex;

- (d) incubating said at least one amplified nucleic acid with said NF-HEV polypeptide;
- (e) isolating a complex between said at least one amplified nucleic acid and said NF-HEV polypeptide;
- (f) repeating steps (c), (d) and (e) a plurality of times; and
- (g) determining the sequence of said nucleic acid in said complex.

123. A method of identifying a compound which inhibits the ability of a NF-HEV polypeptide to bind to a nucleic acid comprising:

(a) incubating a NF-HEV polypeptide or a fragment thereof which recognizes a binding site in a nucleic acid with a nucleic acid containing said binding site in the presence or absence of a test compound; and

(b) determining whether the level of binding of said NF-HEV polypeptide to said nucleic acid in the presence of said test compound is less than the level of binding in the absence of said test compound.

124. A method of assessing NF-HEV activity in a biological sample, said method comprising the steps of:

(a) contacting a nucleic acid molecule comprising a binding site for a NF-HEV polypeptide with a biological sample from a subject or a NF-HEV polypeptide isolated from a biological sample from a subject, the polypeptide comprising the amino acid sequences of one of SEQ ID NOs: 4-5; and

(b) assessing the binding between said nucleic acid molecule and a NF-HEV polypeptide, wherein a detection of decreased binding compared to a reference NF-HEV nucleic acid binding level indicates that said sample comprises a deficiency in NF-HEV activity.

125. A method of identifying a candidate inhibitor of NF-HEV activity, said method comprising:

(a) providing a NF-HEV polypeptide of SEQ ID NOs: 4-5 or, a fragment comprising a contiguous span of at least 6 contiguous amino acids of a polypeptide according to SEQ ID NOs: 4-5;

(b) providing a NF-HEV target polypeptide or a fragment thereof; and

(c) determining whether a test compound selectively inhibits the ability of said NF-HEV polypeptide to bind to said NF-HEV target polypeptide, wherein a determination that said test compound selectively inhibits the ability of said NF-HEV polypeptide to bind to said

NF-HEV target polypeptide indicates that said compound is a candidate inhibitor of NF-HEV activity.

126. The method of any one of Claims 1, 14, 23 or 33, wherein said NF-HEV polypeptide or biologically active fragment thereof comprises an amino acid sequence selected from the group consisting of amino acids 1-65 of SEQ ID NOs: 4-6.